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10/533,700	10/28/2005	Toshiyuki Takai	4439-4032	6164

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EXAMINER

SINGH, ANOOP KUMAR

ART UNIT PAPER NUMBER

1632

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/533,700	TAKAI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 6-8 is/are pending in the application.
- 4a) Of the above claim(s) 6-8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☒ Claim(s) 6-8 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____                                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/26/05</u>   | 6) <input type="checkbox"/> Other: ____                           |

## **DETAILED ACTION**

Applicant's amendment to the specification and claims filed on April 26, 2005, has been received and entered. Claims 4-5 have been canceled, while claims 1-3 and 6-7 have been amended. Claims 1-3 and 6-8 are pending.

### ***Claim Objections***

Claims 6-8 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. In the instant case, claims 6-7 are dependent on a multiple dependent claim 3. It is noted that claim 8 depends on claim 6 or 7 which is indirectly dependent on another multiple dependent claim 3. See MPEP § 608.01(n). Accordingly, the claims 6-8 have not been further treated on the merits.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunizing a transgenic mouse model comprising a homozygous disruption of the exon encoding S2 and EC1 of the FC $\gamma$ RIIB

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gene such that no functional FC $\gamma$ RIIB proteins is produced with gangliosides GQ1b, wherein immunization of said mouse with GQ1b shows peripheral neuropathy consistent with paralysis to its tail and hind legs, does not reasonably provide enablement for a model of Guillain-Barre syndrome (GBS) or Fisher syndrome or deficiency of the FC $\gamma$ RIIB gene or any other "mouse" showing phenotype as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ 1400, 2d at 1404. Such factors are: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the art; (4) The level of one of ordinary skill in the art; (5) The level of predictability in the art; (6) The amount of direction and guidance provided by Applicant; (7) The existence of working examples; and (8) The quantity of experimentation needed to make and/or use the invention.

The office has analyzed the specification in direct accordance to the factors outlines in *In re Wands*. MPEP 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on factors discussed in MPEP 2164.01(a) and the evidence as whole, it is not necessary to discuss each factor in written enablement

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rejection.” These factors will be analyzed, in turn, to demonstrate that one of ordinary skill in the art would have had to perform “undue experimentation” to make and/or use the invention and therefore, applicant’s claims are not enabled.

Claims 1-7 and 32-33 are broad in scope. The following paragraph will outline the full scope of the claims.

Claimed invention recites a mouse model of GBS that can be obtained by immunizing an FCgRIIB gene deficient mouse with gangliosides GQ1b. As recited claims embrace immunizing homozygous as well as heterozygous FCgRIIB gene deficient mouse. Claim 2 is directed to a mouse model of GBS that is Fisher syndrome encompassing any mouse showing phenotype consistent with GBS or Fisher syndrome. Claim 3 limits the mouse model of claims 1 and 2 to include GBS that develops in peripheral and paralysis of its tail and hind legs

Since these claims are broad in scope, encompassing immunizing either heterozygous or homozygous mouse that could be used as animal model for GBS or Fisher syndrome. The disclosure provided by the applicant, in view of prior art, must encompass a wide area of knowledge to a reasonably comprehensive extent. In other word each of those aspect considered broad must be shown to a reasonable extent so that one of the ordinary skill in the art at the time of invention by applicant, would be able to practice the invention without any undue burden being on such Artisan.

The specification broadly describes GBS as inflammatory demyelinating disorder of peripheral nerves that is characterized by rapidly progressing flaccid motor paralysis, loss of deep tendon reflexes, dysphagia, articulatory disorder, deep sensory disturbance

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and vegetative necrosis (see page 1). It is noted that the specification also teaches Fisher syndrome is same as GBS (see page 3, para. 2, of the specification). The specification discloses immunizing Fc $\gamma$ RIIB deficient mice with ganliosides to generate GBS system (see page 5, last para). Page 6-7 describes brief disclosure of the invention and provides brief description of drawing. Page-8-11 broadly describes the best mode of carrying the invention to obtain a mouse model of GBS. Remaining specification describes the specific example of the mouse carrying characteristics similar to one described in this office action. Example 1: of specification teaches immunization of FC $\gamma$ RIIB knockout mice with GQ1b. The FC $\gamma$ RIIB $^{-/-}$  mice immunized with GQ1b show peripheral neuropathy including paralysis of their tail and hind legs (see page 14 of the specification). Example 2 shows that FC $\gamma$ RIIB $^{-/-}$  mice immunized with GQ1b show GBS as compared to wild type control. Example 3 shows that FC $\gamma$ RIIB $^{-/-}$  mice immunized with GQ1b show increased level of IgG1, IgG2a and IgG2b antibody against GQ1b as compared to wild type mice (see page 15 and Figure 3). It is noted that specification describes that FC $\gamma$ RIIB transgenic mouse can be generated by substituting the exon S2 and EC1 with a neo gene cassette (see page 12, paragraph 3 of the specification and also evidenced by Takai, Nature, 1996, 379, 346-349, IDS; see figure 1a).

However, such broad disclosure does not demonstrate the information required by the Artisan to reasonably predict disclosed phenotype in any Fc $\gamma$ RIIB deficient mouse. The specification does not provide any specific guidance as to how a heterozygous mouse or any other mouse would show the same peripheral neuropathy

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after immunization with GQ1b. In fact, Applicant's examples only describe a homozygous FcγRIIB -/- mouse immunized with GQ1b showing spreading of hind legs, inability of walking and dropping tail (claim 1, page 14, para. 1). At the time of the invention, although many of the methods are routine, neither art of record nor the specification teaches how to practice the claimed invention for heterozygous FcγRIIB +/- mouse as recited in the claimed invention. Furthermore, the specification does not teach any other genetic disruption involving FcγRIIB gene. Therefore, it is apparent that any other genetic disruption including substitution or substitution of other exons will not result in same phenotype. It is noted that the specification as filed does not provide any specific information for practicing the claimed mouse model except the FcγRIIB -/- knockout mouse model and peripheral neuropathy associated with the immunization of instant mouse with GQ1b. An artisan would have to carry out extensive experimentation to make and use the invention in immunizing FcγRIIB -/- knockout mouse or any other mouse with partial deletion in the genome to show that it would also result in peripheral neuropathy. These experiments would have been undue because of the art of making transgenic mice without any specific phenotype to study diseases model were unpredictable and specification fails to provide any guidance as to how the claimed method would have been practiced.

Claims 1-3 encompass GBS mouse model by immunizing an FcγRIIB -/- mouse with GQ1b primarily due to deficiency in FcγRIIB gene. The specification only teaches the phenotype after immunizing FcγRIIB-/- null homozygous mouse. It is emphasized that, Holschneider et al. (Int J Devl Neuroscience, 2000, 18: 615-618) state that single

genes are often essential in a number of different physiological processes. Hence deletion of an individual gene in the instant case DOCK2 in mouse may prove so drastic or so widespread as to create an amalgam of phenotypes whose interpretation becomes confounded by the interaction of various new physiologic changes (pp 615). Holschneider et al discuss various factors that contribute to the resulting phenotype of transgenic mice, including compensatory system that may be activated to mask the resulting phenotype; these compensatory changes may be due to differential expression of another gene, which may be regulated by the downstream product of the deleted gene. It is not apparent how skilled artisan without any undue experimentation, practices method as contemplated by the instant claims particularly given the unpredictability of the resulting phenotype of a mouse due to deletion of gene. In the instant case, it is not apparent whether partial deletion of Fc $\gamma$ RIIB would result in the peripheral neuropathy as contemplated by the claims. In fact prior art recognizes that the resultant phenotype, when producing knockdown mice, is exceedingly unpredictable. Griffiths (Microscopy Research and Technique 1998, 41: 344-358) taught that, despite a known role for the PLP gene based on spontaneous mutations in the gene, the knockout mouse failed to display any of the expected phenotype (pp 350, last paragraph). Therefore, the specification does not enable for any other mouse whose Fc $\gamma$ RIIB gene function is deficient other than the transgenic mouse model comprising a homozygous disruption of FC $\gamma$ RIIB that is specifically disclosed in the instant application having the disclosed phenotypes.



Claims 2 and 3 embrace any mouse as a model for GBS or Fisher syndrome; subsequently limiting to a mouse that develops peripheral neuropathy consistent with paralysis of its tail and hind legs. The specification teaches that an inflammatory demyelinating disorder of peripheral nerves which occurs a few weeks after a flu-like symptom, and is characterized by rapidly-progressing flaccid-motor paralysis (weakness in muscles of all four limbs), loss of deep tendon reflexes, dysphagia, articulatory disorder, deep sensory disturbance, and vegetative neurosis (cardiac arrhythmia, blood pressure fluctuation) (see page 1, paragraph 2). In addition, specification also broadly discloses that Fisher syndrome is known as a variant of GBS. It is noted that specification describes the symptoms of Fisher syndrome that includes external ophthalmoplegia, diplopia, ataxia, loss of tendon reflexes, and facial nerve palsy, with a preceding infection of the upper respiratory tract. It is noted that immunization of mice with GQ1b shows peripheral neuropathy and paralysis of tail and hind legs but fails to provide any evidence that these mouse show characteristic consistent with other symptoms of GBS or Fisher syndrome such as weakness in forelimb, dysphagia, articulatory disorder, deep sensory disturbance, and vegetative neurosis (cardiac arrhythmia, blood pressure fluctuation. It is emphasize that syndrome is defined as the aggregate of symptoms and signs associated with any morbid process, and constituting together the picture of the disease (See Stedman's Medical Dictionary 27th Edition). In the instant case, the specification only teaches mouse immunized with GQ1b show paralysis or tail and hind limbs without showing any other symptoms or any histopathology of any demylination consistent with GBS or

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Fisher syndrome. Prior to instant invention, art teaches that even intra dermal inoculation of mouse with HSV-1 shows symptoms such as hind-limb paralysis, flaccid tail and loss of bladder control within 6-7 days post infection (see abstract, Reinhard et al Adv Exp Med Biol. 1996; 398:241-6). Kennel et al (Neurobiol Dis. 1996; 3(2):137-47) also teach a mouse autosomal recessive mutation progressive motor neuronopathy (pmn) that results in early onset motor neuron disease with rapidly progressive hindlimb paralysis, severe muscular wasting, and death at around 6 weeks of age (see page 141, col. 2). These studies suggest that hind limb or tail paralysis cannot be solely rely as phenotype for GBS or any specific syndrome. An artisan would have to perform undue experimentation to determine other symptoms in the instantly claimed mouse model to determine whether this could in fact be a model for any syndrome.

In conclusion, in view of breadth of the claims and absence of a strong showing by the Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by the Applicant is not enabled for the claimed inventions commensurate in scope with these claims. The specification and prior art do not teach a mouse model that would be GBS or Fisher mouse model. An artisan of skill would have required undue experimentation to practice the method as claimed as supported by the observations in the art record.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite to the extent that preamble is not consistent with the rest of the body of the claim. In the instant case, preamble recite a mouse model for Guillain-Barre syndrome while rest of the claim recites immunizing a mouse whose FcγRIIB gene function is deficient in its chromosome to develop Guillain-Barre syndrome. It unclear how a mouse not capable for developing Guillain-Barre syndrome would be useful in a mouse model for Guillain-Barre syndrome since these knockout mouse do not develop this syndrome. Claim 1 is further vague and indefinite to extent it recite a mouse model which "can be obtained" by immunizing...It appears that it is a possibility to obtain a mouse by immunization with GQ1b. The meets and bounds of the recitation of "can be obtained" is not clear. If such a mouse model can be obtained what are the conditions under which it could or couldn't be obtained. Claim 1 is further unclear because it recite a limitation "whose FcγRIIB gene function is deficient in its chromosome". Since the function of a gene cannot be deficient on a chromosome, the meets and bounds of this limitation is unclear. Clams 2-3, 6-8 depends on claim 1. Appropriate correction is required.

Claim 3 recite a limitation wherein mouse model of Guillain-Barre syndrome develops peripheral neuropathy and paralysis of its and hind legs occurs. As recited claim 3 is vague to an extent it does not recite how and under what conditions it

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develops peripheral neuropathy. The meets and bounds of conditions under which it develops peripheral neuropathy and paralysis of hind legs is not clear. Appropriate correction is required.

Claim 3 recites a limitation "according to" that simply requires bringing into agreement. Since, according only implies a level of agreement between two, thus meets and bound of instant claim 3 is unclear and this limitation does not further limit the instant claim. It is emphasized that specific reference to the mouse will obviate this rejection. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Reinhard et al Adv Exp Med Biol. 1996; 398:241-6.

It is noted that claims 2 is drawn to a mouse model of GBS which is fisher syndrome. Claim 3 limits the mouse of claim 2 that develops paralysis of its tail and hind legs. Given the broadest reasonable interpretation these mouse are only characterized by these two phenotype and do not have any structural requirement.

Reinhard taught a mouse that shows symptoms such as hind-limb paralysis, flaccid tail and loss of bladder control, which is obtained by intra dermal inoculation of

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mouse with HSV-1 (see abstract, page 243, para. 1). The mouse disclosed by Reinhard and those embraced by the instant claims appear to be structurally same. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433.

Where, in the instant cases, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

Further see MPEP § 2113, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (Citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal

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carboxylate is not directly added, but is instead produced in-situ does not change the end product.).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takai et al (Nature, 1996, 379, 346-348, IDS), Yuki (Ann Neurol, 2001, 49, 712-720) and Odaka et al (J Neurol Neurosurg Psychiatry. 2001; 70(1): 50-5).

Takai et al teach deletion of FcγRIIB gene in mice results elevated immunoglobulin levels in response to both thymus-dependent and thymus-independent antigens (see abstract). Takai et al teach that the FcγRIIB gene encodes a low affinity immunoglobulin-G receptor that acts as a general negative regulator of immune complex triggered immune system activation. It is noted that loss of this negative regulator increased humoral and anaphylactic response in the mice because the mice lack ability for regulation of antibody in response to antigenic stimulation. Takai et al also indicate that defects in FcγRIIB function may therefore contribute to the development of autoimmunity by a failure of feedback inhibition to regulate antibody production (see page 347, col. 1, para2). However, Takai et al differed from claimed invention by not teach immunizing these mouse with Gangloside GQ1b.

Prior to instant invention, Yuki et al teach immunizing Japanese white rabbit with brain ganglioside and GM1 causing GBS characterized by limb weakness (see page 712, col. 2, para. 2 and figure 1). It is noted that these rabbits could not maintain normal standing position, head or body showing the symptoms of GBS (see page 715, Figure 1a-b). While Yuki et al described the potential of animal model of axonal GBS by immunization with GMQ and BBG Yuki et al differed from claimed invention by not teaching immunization of animal with ganglioside GQ1b.

However, at the time the claimed invention was made, role of other ganglioside such as GQ1b was routine in the art. Odaka et al disclose that patient of Miller Fisher syndrome and GBS had serum IgG antibody to GQ1b ganglioside during the acute phase of the illness (see page 50. col. 2, lines 8-10). It is noted that Odaka et al disclose that a single strain of *C jejuni* has several lipopolysaccharides that bear epitopes common to such gangliosides as GM1, GD1a, and GQ1b (See page 54, col. 2, para 3, also see references therein). Odaka et al teach infection by a strain of *C. jejuni* may induce not only anti-GQ1b IgG, but also anti-GM1 or anti-GD1a IgG in some patients with Fisher or GBS. Odaka also show that one patients *C jejuni* is isolated from a patient with MFS/GBS who has anti-GQ1b and anti-GD1a IgG antibodies. It is noted that Odaka et al compared the frequency of these different ganglioside (see page 54, col. 2, para. 3). However, Odaka et al do not teach immunizing any mouse for a mouse model for GBS or fisher syndrome.

Accordingly, in view of the teachings of Takai, Yuki and Odaka, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was

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made, to immunize the FcγRII knockout disclosed by Takai with ganglioside as taught by Yuki. The skilled artisan would be motivated to use different gangliosides including GQ1b as Odaka taught they all were known antigen that induce anti-GQ1b IgG, anti-GM1 or anti-GD1a IgG antibody in patient infected with single strain of *C jejuni* having several lipopolysaccharides with epitopes common to gangliosides such as GM1, GD1a, and GQ1b (supra). One of ordinary skill in the art would be motivated to combine the teaching of Takai, Yuki and Odaka because it was known in the art that immunization with ganglioside would cause symptoms of GBS or Fisher syndrome and that the FcγRIIB knockout mouse lack a negative regulatory response to various antigen that may contribute to the development of autoimmunity. This is particularly important since Yuki could not immunize wild type rodents with ganglioside to produce GBS symptoms (Yuki et al page 712, col. 2, lines 3). Therefore, given that FcγRIIB knockout mouse and GQ1b and other ganglioside were available for use to immunize as per the teachings of Yuki it would have obvious for an artisan to use the mouse of Takai to immunize with other Ganglioside to produce GBS or Fisher syndrome as disclosed in the instant application.

One who would practiced the invention would have had reasonable expectation of success because Takai had already described advantage of using FcγRIIB knockout mouse to study autoimmunity, while Yuki taught a animal model by immunizing animal with ganglioside. Odaka had already described that a single strain of *C jejuni* having several lipopolysaccharides with epitopes common to gangliosides such as GM1, GD1a, and GQ1b. Thus, it would have only required routine experimentation to immunize the



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mouse taught by Takai with GQ1b to make a mouse showing symptoms consistent with GBS as required by instant invention.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

### ***Conclusion***

No Claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bowes et al (Infection and Immunity, 2002, 70(9), 5008-5018).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272- 0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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